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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,530	07/18/2001	Edward B. Skibo	5452-US	4313

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EXAMINER	
KRASS, FREDERICK F	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 11/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/889,530	SKIBO, EDWARD B.	
	Examiner	Art Unit	
	Frederick F. Krass	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *15-17* is/are allowed.

6)☒ Claim(s) *11,14,18 and 21* is/are rejected.

7)☒ Claim(s) *12,13,19,20 and 22* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11-4-2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Previous Rejections

Unless specifically repeated hereinunder, all prior rejections are withdrawn.

Claim Informalities

Claims 13 and 14 should be amended to end in periods.

Scope of Enablement Rejection (New, Necessitated by Applicant's Amendment)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18 and 21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of animal or human subjects afflicted with central nervous system cancer, colon cancer, ovarian cancer and lung cancer, does not reasonably provide enablement for the treatment of animal or human subjects afflicted with "neoplastic disease". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,

4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth hereinbelow.

1. The nature of the invention, state of the prior art, relative skill of those in the art, and the predictability of the art

The claimed invention relates to chemotherapy, and the relative skill of those in the art is high, generally that of a PHD or MD. Conversely, the cancer treatment art involves a very high level of unpredictability. While the state of the art is relatively high with regard to the treatment of specific cancers with specific agents, it has long been underdeveloped with regard to the treatment of cancers broadly. In particular, there is no known anticancer agent which is effective against all cancers. This is why the National Cancer Institute (NCI) has the extensive *in vitro* drug screening program it does. As discussed by the court in In re Brana, 51 F.3d 1560 (Fed. Cir. 1995), *in vitro* assays are used by NCI (such as the P388 and L1210 lymphocytic leukemia tests at issue therein) to measure the potential antitumor properties of a candidate compound. Brana at 1562-63. If success is shown in this initial screening step, this demonstrates that at least one cancer type (e.g., lymphocytic leukemia) is sensitive thereto, and provides the incentive to select it for further studies to determine its usefulness as a chemotherapeutic agent against other cancer types (lung, breast, colon, etc.) *Id.* at 1567-68. These *in vitro* tests are considered reasonably correlative of success *in vivo*.

Moreover, candidate anticancer drugs must also be evaluated for their ability to inhibit metastasis in particular tissue types. See USP 6,448,030 at col. 1, lines 19-28. This patent demonstrates the state of

the art and further illustrates the extensive experimentation necessary to determine the efficacy of candidate anticancer drugs in particular tumor types.

Thus, a considerable amount of *in vitro* empirical testing is required, with no *a priori* expectation of success being present, before a candidate anticancer agent can be considered useful against any particular cancer type. Indeed, this reiterates the very same position taken by Applicant at page 12 of his response.

2. The breadth of the claims

The claim is very broad and inclusive of "neoplastic disease" generally.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction for ascertaining, *a priori*, which tumor types will respond to treatment, other than central nervous system cancer, colon cancer, ovarian cancer and lung cancer, the species actually tested by hollow fiber assay in the working examples.

4. The quantity of experimentation necessary

The lack of adequate guidance from the specification or prior art with regard to the actual treatment of all cancers in a mammal with the claimed compounds fails to rebut the presumption of unpredictability extant in this art. Applicants fail to provide the guidance and information required to ascertain which particular type of cancer the claimed anticancer agent will be effective against without resorting to undue experimentation.

Absent a reasonable *a priori* expectation of success for using a specific chemotherapeutic agent to treat a particular type of cancer, one skilled in the art would have to extensively test many various

tumor types. Since each prospective embodiment, and indeed future embodiments as the art progresses, would have to be empirically tested, and those which initially failed tested further, an undue amount of experimentation would be required to practice the invention as its is claimed in its current scope, because the specification provides inadequate guidance to do otherwise.

Anticipation Rejection

Claims 1-7 were rejected under 35 U.S.C. 102(b) as being anticipated by Skibo et al (J. Med. Chem., vol. 40, pp. 1327-1339).

This rejection is maintained and is now applicable to claims 11 and 14.

Applicant states:

> The Office Action seems to urge that methanol and buffer solutions for enzymatic in vitro studies as discussed in the Skibo publication anticipate the Applicant's claims to its pharmaceutical preparation for treating neoplastic disease. It is respectfully requested that the Patent Office advise where in the prior art one is taught to use a buffer solution for an enzymatic assay for administration to an animal or human.

Applicant misunderstands the examiner's position. The examiner is not proposing that the prior art discloses administration to an animal or human. The instant claims do not require such administration; rather, they recite pharmaceutical compositions capable of that intended use. The prior art methanol and buffer solutions are also capable of being used for that same purpose (whether the prior art recognizes such uses or not), and thus anticipate the instantly claimed subject matter.

Allowable Subject Matter

Claims 15-17 are allowable as presently advised.

Claims 12, 13, 19, 20 and 22 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The prior art of record does not fairly suggest, teach or disclose the specific compounds of claims 16 and 17, i.e. Yujungamycin B and Yujungamycin C, nor pharmaceutical compositions comprising same, nor the treatment of central nervous system cancer, colon cancer, ovarian cancer or lung cancer therewith in animal or human subjects.

The prior art of record also does not fairly suggest, teach or disclose the use the known compound Yujungamycin A to treat central nervous system cancer, colon cancer, ovarian cancer or lung cancer in animal or human subjects.

Action is Final

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frederick F. Krass whose telephone number is 571-272-0580. The examiner's schedule is as follows:

Monday: 10:30AM- 7PM;
Tuesday: 10:30AM - 7PM;
Wednesday: off;

Thursday: 10:30AM- 7PM; and
Friday: 10:30AM-7PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached at 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Frederick Krass
Primary Examiner
Art Unit 1614